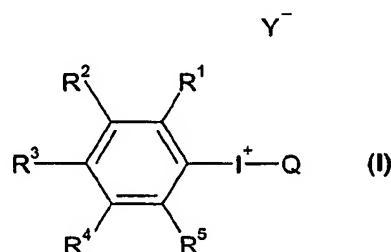


Claims

- 1) A method for the production of an aromatic fluorine-labelled compound comprising fluoridation of an iodonium salt with a fluoride ion source characterised in that the reaction mixture contains a free radical trap.
- 2) The method of claim 1 wherein the free radical trap is selected from 2,2,6,6-Tetramethylpiperidine-N-Oxide, 1,2-diphenylethylene, ascorbate, para-amino benzoic acid, α -tocopherol, hydroquinone, di-t-butyl phenol, β -carotene and gentisic acid.
- 3) The method of either of claims 1 or 2 wherein the free radical trap is 2,2,6,6-Tetramethylpiperidine-N-Oxide or 1,2-diphenylethylene.
- 4) The method of any of claims 1-3 wherein the fluoride ion source is selected from potassium fluoride, caesium fluoride and tetraalkylammonium fluoride.
- 5) The method of claim 4 wherein the fluoride ion source is potassium fluoride and KryptofixTM is used to activate the fluoride ion.
- 6) The method of any of claims 1-5 wherein the iodonium salt is of Formula I:



wherein:

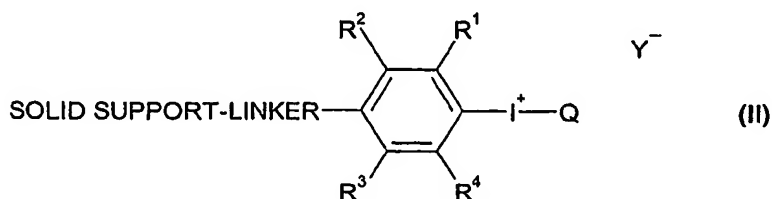
Q is a precursor of the fluorine-labelled compound ;

R¹-R⁵ are independently selected from hydrogen, nitro, cyano, halogen, C₁₋₁₀ hydroxyalkyl, C₂₋₁₀ carboxyalkyl, C₁₋₁₀ alkyl, C₂₋₁₀ alkoxyalkyl, C₁₋₁₀ hydroxyalkyl, C₁₋₁₀ aminoalkyl, C₁₋₁₀ haloalkyl, C₆₋₁₄ aryl, C₃₋₁₂ heteroaryl, C₃₋₂₀ alkylaryl, C₅₋₁₂ arylene, C₂₋₁₀ alkenyl, C₂₋₁₀ alkynyl, C₁₋₁₀ acyl, C₇₋₁₀ aroyl, C₂₋₁₀ carboalkoxy, C₂₋₁₀ carbamoyl, C₂₋₁₀ carbamyl, or C₁₋₁₀ alkylsulphinyl, or protected versions of any of

these groups; or alternatively forms a four- to six-membered ring together with the R group to which it is adjacent, or protected versions thereof; and,

Y^- is an anion selected from triflate, nonaflate, mesylate and hexaflate.

- 7) The method of any of claims 1-5 wherein the iodonium salt is solid support-bound as in Formula II:

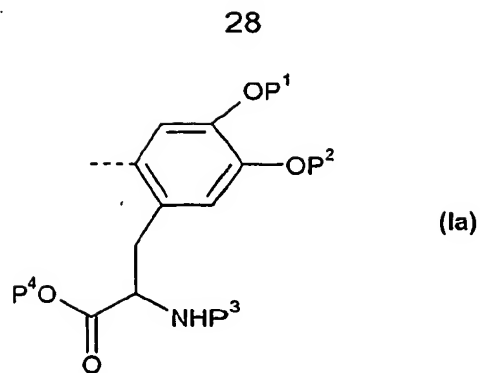


wherein:

Q is a precursor of the fluorine-labelled compound; and,

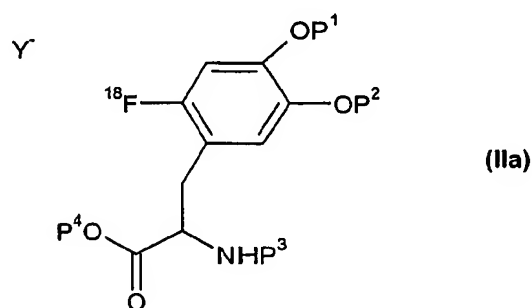
R^1 - R^4 and Y^- are as defined for Formula I of claim 6.

- 8) The method of either of claims 6 or 7 wherein Q is an aryl group optionally substituted by 1 to 5 substituents independently selected from nitro, cyano, halogen, C_{1-10} hydroxyalkyl, C_{2-10} carboxyalkyl, C_{1-10} alkyl, C_{2-10} alkoxyalkyl, C_{1-10} hydroxyalkyl, C_{1-10} aminoalkyl, C_{1-10} haloalkyl, C_{6-14} aryl, C_{3-12} heteroaryl, C_{3-20} alkylaryl, C_{5-12} arylene, C_{2-10} alkenyl, C_{2-10} alkynyl, C_{1-10} acyl, C_{7-10} aroyl, C_{2-10} carboalkoxy, C_{2-10} carbamoyl, C_{2-10} carbamyl, or C_{1-10} alkylsulphinyl, or protected versions of any of these groups; or alternatively forms a four- to six-membered ring together with the R group to which it is adjacent, or protected versions thereof.
- 9) The method of any of claims 1-8 wherein the fluorine-labelled compound is an $[^{18}F]$ -labelled compound and the fluoride ion source is a source of $^{18}F^-$.
- 10) The method of claim 9 wherein the $[^{18}F]$ -labelled compound is $[^{18}F]$ -FDOPA.
- 11) The method of any of claims 6-10 wherein the precursor is of Formula Ia:



wherein P^1 , P^2 , P^3 , and P^4 are each independently hydrogen or a protecting group;

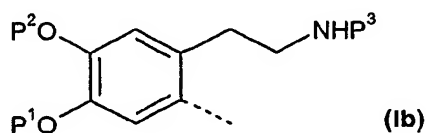
said method producing the labelled compound of Formula IIa:



- 5 wherein P^1 , P^2 , P^3 , and P^4 are each independently hydrogen or a protecting group and Y^- is an anion, preferably trifluoromethylsulphonate (triflate) anion.

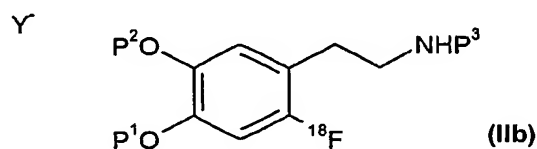
12) The method of claim 9 wherein the [^{18}F]-labelled compound is [^{18}F]-dopamine.

13) The method of any of claims 6-10 and 12 wherein the precursor is of Formula Ib:



- 10 wherein P^1 , P^2 , and P^3 are each independently hydrogen or a protecting group;

said method producing the labelled compound of Formula IIb:

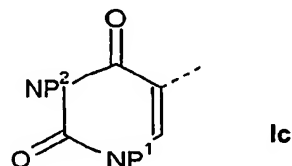


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wherein P^1 , P^2 , and P^3 are each independently hydrogen or a protecting group and Y^- is an anion, preferably trifluoromethylsulphonate (triflate) anion.

14) The method of claim 9 wherein the [^{18}F]-labelled compound is [^{18}F]-uracil.

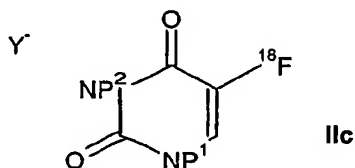
15) The method of any of claims 6-10 and 14 wherein the precursor is of Formula Ic:



5

wherein P^1 and P^2 are each independently hydrogen or a protecting group;

said method producing the labelled compound of Formula IIc:



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wherein P^1 and P^2 are each independently hydrogen or a protecting group and Y^- is an anion, preferably trifluoromethylsulphonate (triflate) anion.

16) The method of any of claims 9-15, further comprising:

- (i) removal of excess $^{18}\text{F}^-$, for example by ion-exchange chromatography; and/or
- (ii) removal of the protecting groups; and/or
- (iii) removal of organic solvent; and/or
- (iv) formulation of the resultant compound as an aqueous solution.

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17) An [^{18}F]-labelled compound produced by the method of any of claims 1-16.